

Application No. 10/699,517  
Amendment dated July 1, 2005  
Reply to Office Action of April 7, 2005

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings of claims in the application:

**Listing of Claims:**

1. (Withdrawn from Consideration) A method of preventing or treating a disease characterized by Lewy bodies or alpha-synuclein aggregation in the brain, the method comprising  
administering an effective regime of an agent that induces an immunogenic response against alpha-synuclein to a patient.
2. (Withdrawn from Consideration) The method of claim 1, wherein the immunogenic response comprises antibodies to alpha synuclein.
3. (Withdrawn from Consideration) The method of claim 1, wherein the agent is alpha-synuclein.
4. (Withdrawn from Consideration) The method of claim 1, wherein the agent is an immunogenic fragment of alpha-synuclein.
5. (Withdrawn from Consideration) The method of claim 4, wherein the immunogenic fragment is amino acid residue 35-65 of alpha-synuclein (SEQ ID NO: 1).
6. (Withdrawn from Consideration) The method of claim 4, wherein the immunogenic fragment comprises amino acid residues 130-140 of alpha-synuclein (SEQ ID NO: 1) and has fewer than 40 amino acids total.
7. (Withdrawn from Consideration) The method of claim 4, wherein the C-terminal amino acid of the fragment is the C-terminal amino acid of alpha-synuclein.

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8. (Withdrawn from Consideration) The method of claim 1, further comprising determining that a patient is suffering from or at risk of a disease characterized by Lewy bodies, wherein the determining step occurs before the administration step.

9. (Withdrawn from Consideration) The method of claim 8, wherein the determining step determines that a patient is suffering from a clinical symptom of a disease characterized by Lewy bodies.

10. (Withdrawn from Consideration) The method of claim 8 or 9, further comprising determining the patient is free of clinical symptoms of a disease characterized by amyloid deposits of A $\beta$ .

11. (Withdrawn from Consideration) The method of claim 3, wherein the alpha-synuclein is administered with an adjuvant.

12. (Withdrawn from Consideration) The method of claim 4, wherein the immunogenic alpha-synuclein fragment is administered with an adjuvant.

13. (Withdrawn from Consideration) The method of claim 3, wherein the alpha-synuclein is linked to a carrier molecule to form a conjugate.

14. (Withdrawn from Consideration) The method of claim 13, wherein the alpha-synuclein is linked to the carrier molecule at the N-terminus of the alpha-synuclein.

15. (Withdrawn from Consideration) The method of claim 4, wherein the immunogenic alpha-synuclein fragment is linked to a carrier molecule to form a conjugate.

16. (Withdrawn from Consideration) The method of claim 15, wherein the immunogenic alpha-synuclein fragment is linked to the carrier molecule at the N-terminus of the immunogenic alpha-synuclein fragment.

17. (Withdrawn from Consideration) The method of claim 1, wherein the agent is an antibody to alpha-synuclein or a fragment thereof.

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18. (Withdrawn from Consideration) The method of claim 17, wherein the antibody is a humanized antibody.

19. (Withdrawn from Consideration) The method of claim 17, wherein the antibody is human

20. (Withdrawn from Consideration) The method of claim 18 or 19, wherein the antibody is an antibody of human IgG1 isotype.

21. (Withdrawn from Consideration) The method of claim 17, wherein the antibody is a monoclonal antibody.

22. (Withdrawn from Consideration) The method of claims 17, wherein the antibody is a polyclonal antibody.

23. (Withdrawn from Consideration) The method of claim 17, wherein the antibody is prepared from a human immunized with alpha-synuclein peptide.

24. (Withdrawn from Consideration) The method of claim 23, wherein the human is the patient to be treated with antibody.

25. (Withdrawn from Consideration) The method of claim 17 or 18, wherein the antibody is administered with a pharmaceutical carrier as a pharmaceutical composition.

26. (Withdrawn from Consideration) The method of claim 17, wherein the antibody is administered at a dosage of 0.0001 to 100 mg/kg, preferably, at least 1 mg/kg body weight antibody.

27. (Withdrawn from Consideration) The method of claim 17, wherein the antibody is administered in multiple dosages over a prolonged period, for example, of at least six months.

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28. (Withdrawn from Consideration) The method of claim 17, wherein the antibody is administered as a sustained release composition.

29. (Withdrawn from Consideration) The method of claim 17, wherein the antibody is administered intraperitoneally, orally, subcutaneously, intracranially, intramuscularly, topically, intranasally or intravenously.

30. (Withdrawn from Consideration) The method of claim 17, wherein the antibody is administered by administering a polynucleotide encoding at least one antibody chain to the patient.

31. (Withdrawn from Consideration) The method of claim 30, wherein the polynucleotide is expressed to produce the antibody chain in the patient.

32. (Withdrawn from Consideration) The method of claim 31, wherein the polynucleotide encodes heavy and light chains of the antibody and the polynucleotide is expressed to produce the heavy and light chains in the patient.

33. (Withdrawn from Consideration) The method of claim 17, further comprising monitoring the patient for level of administered antibody in the blood of the patient.

34. (Withdrawn from Consideration) The method of claim 17, wherein the antibody is internalized within neuronal cells having Lewy bodies thereby dissipating the Lewy bodies.

35. (Withdrawn from Consideration) The method of claim 17, wherein the antibody binds to the outer surface of neuronal cells having Lewy bodies thereby dissipating the Lewy bodies.

36. (Withdrawn from Consideration) The method of any one of claims 1-4 or 17, further comprising administering to the patient an effective regime of an agent that induces an immunogenic response against A $\beta$ .

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37. (Withdrawn from Consideration) The method of claim 36, wherein the agent is A $\beta$  or an immunogenic fragment thereof.

38. (Withdrawn from Consideration) The method of claim 36, wherein the agent is an antibody to A $\beta$  or a fragment thereof.

39. (Withdrawn from Consideration) The method of claim 36, wherein the disease is Parkinson's disease.

40. (Withdrawn from Consideration) The method of claim 36, wherein the patient is free of Alzheimer's disease and has no risk factors thereof.

41. (Currently Amended) A method of therapeutically treating a patient suffering from a disease characterized by Lewy bodies or alpha-synuclein aggregation in the brain, the method comprising

administering to the patient an effective regime of an agent that induces an immunogenic response against A $\beta$  in the patient and thereby therapeutically treating the disease, wherein the disease is selected from the group consisting of Parkinson's disease, Dementia with Lewy Bodies (DLB), Diffuse Lewy Body Disease (DLBD), Pure Autonomic Failure, Lewy Body Dysphagia, Incidental Lewy Body Disease, Inherited Lewy Body Disease, and Multiple System Atrophy

wherein the agent is is A $\beta$  or an immunogenic fragment thereof, or is an antibody to A $\beta$ .

42. (Previously Presented) The method of claim 41, wherein the agent is A $\beta$  or an immunogenic fragment thereof.

43. (Currently Amended) The method of claim 41, wherein the agent is an antibody to A $\beta$  ~~or a fragment thereof.~~

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44. (Previously Presented) A method of therapeutically treating a patient suffering from a disease characterized by Lewy bodies or alpha synuclein deposits in the brain, comprising

administering to the patient an effective regime of an agent that induces an immunogenic response against alpha-synuclein and an agent that induces an immunogenic response against A $\beta$  in the patient and thereby therapeutically treating the disease, wherein the disease is selected from the group consisting of Parkinson's disease, Dementia with Lewy Bodies (DLB), Diffuse Lewy Body Disease (DLBD), Pure Autonomic Failure, Lewy Body Dysphagia, Incidental Lewy Body Disease, Inherited Lewy Body Disease, and Multiple System Atrophy;  
wherein the agent that induces an immunogenic response against alpha-synuclein is alpha synuclein or an immunogenic fragment thereof or an antibody to alpha synuclein, and the agent that induces an immunogenic response against A $\beta$  is A $\beta$  or an immunogenic fragment thereof, or an antibody to A $\beta$ .

45. (Previously Presented) The method of claim 41, wherein the agent is administered peripherally.

46. (Previously Presented) The method of claim 41, wherein the effective regime comprises administering multiple dosages over a period of at least six months.

47. (Canceled)

48. (Previously Presented) The method of claim 41, wherein the patient has a risk factor for the disease.

49. (Canceled)

50. (Previously Presented) The method of claim 41, wherein the disease is Parkinson's disease.

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51. (Previously Presented) The method of claim 50, wherein the patient has Parkinson's disease and the administering results in improvement in a sign or symptom of Parkinson's disease.

52. (Previously Presented) The method of claim 50, wherein the patient has Parkinson's disease, and the administering improves motor characteristics of the patient.

53. (Previously Presented) The method of claim 41, further comprising monitoring a sign or symptom of Parkinson's disease in the patient.

54. (Previously Presented) The method of claim 41, wherein the patient is free of Alzheimer's disease.

55. (Previously Presented) The method of claim 54, wherein the patient is free of Alzheimer's disease and has no risk factors thereof.

56. (Withdrawn from Consideration) A pharmaceutical composition comprising an agent effective to induce an immunogenic response against a component of a Lewy body in a patient.

57. (Withdrawn from Consideration) The pharmaceutical composition of claim 56, wherein the agent is an antibody specific for a component of a Lewy body.

58. (Withdrawn from Consideration) The pharmaceutical composition of claim 56, wherein the agent is alpha-synuclein, an immunogenic alpha-synuclein fragment, 6CHC-1, or an immunogenic 6CHC-1 fragment.

59. (Withdrawn from Consideration) The pharmaceutical composition of claim 56, wherein the agent is an immunogenic alpha-synuclein fragment.

60. (Withdrawn from Consideration) The pharmaceutical composition of claim 59, wherein the immunogenic alpha-synuclein fragment is NAC.

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61. (Withdrawn from Consideration) The pharmaceutical composition of claim 56, further comprising a pharmaceutically acceptable adjuvant.

62. (Withdrawn from Consideration) A method of screening an antibody for activity in preventing or treating a disease associated with Lewy bodies, comprising  
contacting a neuronal cell expressing synuclein with the antibody;  
determining whether the contacting reduces synuclein deposits in the cells compared with a control cells not contacted with the antibody.

63. (Withdrawn from Consideration) A method of screening an antibody for activity in treating or preventing a Lewy body disease in the brain of a patient, comprising  
contacting the antibody with a polypeptide comprising at least five contiguous amino acids of alpha-synuclein; and  
determining whether the antibody specifically binds to the polypeptide, specific binding providing an indication that the antibody has activity in treating the disease.

64. (Withdrawn from Consideration) A method of screening an agent to determine whether the agent has activity useful in treating a disease characterized by Lewy Bodies, comprising  
contacting the agent with a transgenic nonhuman animal disposed to develop a characteristic of a Lewy Body disease with the agent;  
determining whether the agent affects the extent or rate of development of the characteristic relative to a control transgenic nonhuman animal;  
wherein the agent is an immunogenic fragment of alpha synuclein or an antibody to alpha synuclein.

65. (Withdrawn from Consideration) The method of claim 64, wherein the transgenic nonhuman animal comprises a transgene expressing alpha-synuclein.

66. (Withdrawn from Consideration) The method of claim 65, wherein the alpha synuclein transgene is full length alpha synuclein.



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67. (Withdrawn from Consideration) The method of claim 64, wherein the transgenic nonhuman animal further comprises a transgene expressing amyloid precursor protein.

68. (Withdrawn from Consideration) The method of claim 36, wherein the administering of the agent inducing an immunogenic response to alpha-synuclein and the agent inducing an immunogenic response to A $\beta$  is simultaneous, separate, or sequential.

69. (Withdrawn from Consideration) The pharmaceutical composition of claims 56, wherein the agent is linked to a carrier molecule to form a conjugate.

70. (Withdrawn from Consideration) The pharmaceutical composition of claims 56, further comprising an agent effective to induce an immunogenic response against A $\beta$ .

71. (Currently Amended) A method of prophylactically treating a patient susceptible to a disease characterized by Lewy bodies or alpha-synuclein aggregation in the brain, the method comprising  
administering to the patient an effective regime of an agent that induces an immunogenic response against A $\beta$  in the patient and thereby effecting prophylaxis of the disease  
wherein the agent is A $\beta$  or an immunogenic fragment thereof, or is an antibody to A $\beta$ .

72. (Previously Presented) The method of claim 71, wherein the agent is A $\beta$  or an immunogenic fragment thereof.

73. (Currently Amended) The method of claim 71, wherein the agent is an antibody to A $\beta$  ~~or a fragment thereof~~.

74. (Currently Amended) A method of prophylactically treating a patient susceptible to a disease characterized by Lewy bodies or alpha synuclein deposits in the brain, comprising

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administering to the patient an effective regime of an agent that induces an immunogenic response against alpha-synuclein and an agent that induces an immunogenic response against A $\beta$  in the patient and thereby effecting prophylaxis of the disease, wherein the disease is selected from the group consisting of Parkinson's disease, Dementia with Lewy Bodies (DLB), Diffuse Lewy Body Disease (DLBD), Pure Autonomic Failure, Lewy Body Dysphagia, Incidental Lewy Body Disease, Inherited Lewy Body Disease, and Multiple System Atrophy

wherein the agent that induces an immunogenic response against alpha-synuclein is alpha synuclein or an immunogenic fragment thereof or an antibody to alpha synuclein, and the agent that induces an immunogenic response against A $\beta$  is A $\beta$  or an immunogenic fragment thereof, or an antibody to A $\beta$ .

75. (Previously Presented) The method of claim 71, wherein the agent is administered peripherally.

76. (Previously Presented) The method of claim 71, wherein the effective regime comprises administering multiple dosages over a period of at least six months.

77. (Canceled)

78. (Previously Presented ) The method of claim 77, wherein the patient has a risk factor for the disease.

79. (Previously Presented) The method of claim 71, wherein the patient is free of Alzheimer's disease.

80. (Previously Presented) The method of claim 79, wherein the patient is free of Alzheimer's disease and has no risk factors thereof.